Citation:

Lindqvist HM, Langkilde AM, Undeland I, Sandberg AS. Herring (*Clupea harengus*) intake influences lipoproteins but not inflammatory and oxidation markers in overweight men. *Br J Nutr.* 2009 Feb;101(3):383-90. Epub 2008 Jul 18.

PubMed ID: 18634706

Study Design:

Randomized Crossover Trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

NEUTRAL: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

This study evaluates the effects of a diet rich in specified, pre-made herring meals on CVD risk factors in healthy, overweight men.

Inclusion Criteria:

- Male
- Employees of the Volvo Car Corporation (Torslanda, Sweden)
- Healthy, no chronic disease
- Willing to eat herring once per day, 5 days/week, for 6 weeks

Exclusion Criteria:

- Use of lipid-lowering drugs or anti-inflammatory drugs
- Ate fish more than 3 times per week or ate functional food products or other foods with high amounts of long-chain *n*-3 PUFA

Description of Study Protocol:

Recruitment

Men from the Volvo Car Corporation volunteered for this study.

Design

The study was a randomized, crossover, intervention study (2x6 weeks), with herring meals for 6 weeks, chicken or lean pork meals for 6 weeks, and a 12-week washout period between the two interventions.

Blinding used (if applicable): not noted

Intervention (if applicable)

Dietary intervention: 150 g raw herring or 150 g raw chicken or 150 g browned pork fillets

Statistical Analysis

- All statistical calculations are comparisons between the two intervention diets made with the paired Student's *t* test and presented as mean values and standard deviations, with significance set at $P<0.05$.
- Microsoft Office Excel, 2003, SP2 (Microsoft Corp., Redmond, WAS, USA) was used for the *t* test and descriptive statistics.
- The Statistical Package for the Social Sciences (SPSS, version 14.0 for Windows; SPSS Inc., Chicago, IL, USA) was used for box plots and for testing with the Wilcoxon signed rank test, when a non-normal distribution was expected.

Data Collection Summary:

Timing of Measurements

Before and after each 6 week intervention.

Dependent Variables

- Plasma cholesterol and plasma TAG concentrations were determined using fully enzymic techniques

Independent Variables

- 150 g baked herring 5 d/week, for 6 weeks
- 150 g baked lean pork or chicken fillet 5 d/week, for 6 weeks

Control Variables

Subjects were asked to maintain their weight during the 25 week period

Description of Actual Data Sample:

Initial N: 40 men

Attrition (final N): 35 subjects completed the study; TAG analysis was excluded for 5 subjects who ate breakfast; C-reactive protein analysis was excluded for 11 subjects who suffered from a cold or had temporary use of anti-inflammatory drugs

Age, Other relevant demographics and Anthropometrics:

Baseline characteristics of 35 subjects

Characteristic	Mean	SD	Range
Age (years)	47.8	6.1	35-60
BMI (kg/m^2)	28.3	2.6	24.7-34.7

Weight (kg)	93.5	9.8	82-127
SBP (mmHg)	124.9	11.7	103-160
DBP (mmHg)	79.7	8.5	63-100
Serum total cholesterol (mmol/l)	5.3	0.79	3.6-6.6
Serum LDL cholesterol (mmol/l)	3.6	0.71	2.2-4.7
Serum HDL (mmol/l)	1.0	0.18	0.7-1.4
Serum TAG (mmol/l)	1.6	0.74	0.7-3.8
Whole-blood AA (g/l)	0.203	0.034	0.15-0.29
Whole-blood DHA (g/l)	0.086	0.018	0.052-0.119
Whole-blood EPA (g/l)	0.035	0.010	0.019-0.071
(EPA+DHA)AA	0.615	0.17	0.33-1.17

Ethnicity: not described

Location:Torslanda, Sweden

Summary of Results:

Key Findings

- HDL was significantly higher after the herring diet period compared with after the reference diet period
- TAG decreased after both diets, with no significant difference between the two diets
- $ORAC_{PCA}$ values did not indicate lower concentrations of non-protein plasma antioxidants
- Oxidized LDL was hot higher after the herring diet than after the reference diet

Biomarkers and risk factors for CVD (Mean values and standard deviations for thirty-five men)

	Baseline Mean	Baseline SD	Reference intervention Mean	Reference intervention SD	Herring intervention Mean	Herring intervention SD
Weight (kg)	93.5	9.8	93.0	9.2	92.5	9.5

Whole-blood arachidonic acid (g/l)	0.203	0.034	0.207	0.034	0.187***	0.029
Whole-blood EPA (g/l)	0.035	0.010	0.029	0.012	0.051***	0.015
Whole-blood DHA (g/l)	0.086	0.018	0.081	0.019	0.106***	0.022
Systolic blood pressure (mmHg)	124.9	11.7	121.2	11.4	123.3	10.4
Diastolic blood pressure (mmHg)	79.7	8.5	78.9	6.1	79.7	7.6
TAG (mmol/l)II	1.58	0.74	1.29*	0.51	1.23*	0.61
Total cholesterol (mmol/l)	5.30	0.79	5.25	0.88	5.33	0.77
LDL (mmol/l)	3.58	0.71	3.69	0.79	3.73	0.66
HDL (mmol/l)	1.00	0.18	0.99	0.21	1.04**	0.23
HDL_2(mmol/l)	0.24	0.11	0.23	0.10	0.26**	0.13
HDL_3(mmol/l)	0.76	0.13	0.76	0.13	0.77	0.17
IL-6(pg/ml)	0.77	0.60	0.54	0.33	0.56	0.39
IL-18(pg/ml)	201	82	193	74	188	74
ICAM-a(ng/ml)	249	44	236	38	237	36
Oxidized LDL (U/l)	69.4	12.0	69.4	12.2	68.8	11.7
CRP (mg/l)[x]	1.94	1.00	1.91	0.89	1.86	0.97
$ORAC_{PCA}$ (mmol Trolox equivalents/l)	1.26	0.11	1.31	0.12	1.32	0.10
Bleeding time (s)	266	60	251	59	256	56

Mean value was significantly different from that for the reference intervention: **P<0.01, ***P<0.00001

*mean value significantly different from that at baseline P<0.05

[x]After excluding values >20, reported cold or intake of acetylsalicylic acid

Author Conclusion:

A 6-week herring-rich diet significantly raised HDL compared with a diet of matched lean pork and chicken dishes. No adverse effects on *in vivo* oxidation or serum antioxidants were found after herring intake.

Reviewer Comments:

Only men studied. Each intervention composed of 150 g/day for 5 days over 6 weeks; unclear if this period of time would affect certain inflammatory and oxidation markers. Sponsored by the National Board of Fisheries.

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	???
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes

2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	???
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes

5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	???
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	???
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	Yes
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	???
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes

8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	Yes
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	N/A
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	???
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	???